REMARKS

The present communication is a supplemental response to the Office Action dated April 20, 2004, in view of the inadvertent failure (in the Response submitted August 12, 2004) to specifically address one of the issues raised in that Office Action. Thus, the rejection under 35 U.S.C. §102(e) over U.S. Patent No. 6,248,559 B1 is specifically addressed at pages 11-13 of this communication. For the Examiner's convenience, the discussion of each of the other issues raised in the Office Action dated April 20, 2004, is reproduced herein (so that this communication addresses, in one document, all of the issues raised in the Office Action dated April 20, 2004).

The present invention relates to co-repressor polypeptides that are capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Exemplary members of the silencing mediators of retinoic acid and thyroid hormone receptors (SMRT) are provided, including various isoforms of human, mouse and Drosophila SMRT co-repressors.

Claims 3-5, 9, 10, 12-14, 16-25 and 38 are currently pending in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination, is presented in the Listing of Claims, beginning on page 2 of this communication, with an appropriate defined status identifier for each claim.

Oath/Declaration

The Examiner's observation that the signature of Inventor Chen is missing from the declaration is noted. This informality will be addressed in due course under separate cover.

35 U.S.C. §112, second paragraph

The rejection of claims 3-5, 9, 10, 12-14, 16-25, and 38 under 35 U.S.C. §112, second paragraph for alleged indefiniteness, is respectfully traversed.

Specifically, Applicants respectfully disagree with the Patent Office's assertion that the phrase "or a peptide portion thereof" allegedly renders claims 4, 5, 9, 12, and 14 indefinite (see page 3, paragraph 3 of the Office Action). Applicants respectfully submit that claims 4, 5, 9, and 12 clearly convey to one of skill what Applicants regard as the invention. Applicants respectfully submit that the present claims (as amended in Applicants' communication submitted August 12, 2004), explicitly recite structural (*i.e.*, an amino acid sequence having at least 80% sequence identity with SEQ ID NOs: 5, 7, or 9) and functional properties (*i.e.*, capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors) for "peptide portions" of SMRT co-repressors. Thus, the present claims embrace any and all polynucleotides encoding a SMRT co-repressor or peptide portion thereof that have the recited structural and functional properties, including, for example, polynucleotides that encode fusion proteins comprising a peptide portion of a SMRT co-repressor provided by the present invention.

With respect to the assertion by the Patent Office that the phrase "said first polynucleotide" in claim 14 lacks prior antecedent basis (see page 3, paragraph 4 of the Office Action), claim 14, as amended in Applicants' communication submitted August 12, 2004, provides antecedent basis for the subject phrase.

Applicants respectfully disagree with the further assertion by the Patent Office that the term "specifically", as used in reference to a hybridizing oligonucleotide in claims 23 and 25, is allegedly vague and indefinite (see page 4, paragraph 1 of the Office Action). One of ordinary skill in the art understands that oligonucleotides that "hybridize specifically" to a particular

polynucleotide do not hybridize to other unspecified polynucleotides under suitable stringent conditions. However, in the interest of advancing prosecution, claim 23 (as amended in Applicants' communication submitted August 12, 2004), explicitly embraces oligonucleotides which hybridize, under suitable stringency conditions, to a specified polynucleotide (*i.e.*, the polynucleotide of claim 4) without hybridizing to comparison polynucleotides (*i.e.*, polynucleotides encoding SEQ ID NO:11 or polynucleotides encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO:5). Additionally, claim 25 (as amended in Applicants' communication submitted August 12, 2004), explicitly embraces oligonucleotides which hybridize, under suitable stringency conditions, to a specified polynucleotide (*i.e.*, polynucleotide encoding SEQ ID NO:5 or SEQ ID NO:7) without hybridizing to comparison oligonucleotides (*i.e.*, polynucleotide encoding SEQ ID NO:9). Thus, the claims (as amended in Applicants' communication submitted August 12, 2004) provide clear guidance as to the stringency of hybridization conditions required, i.e., sufficient stringency to avoid hybridization with polynucleotides encoding SEQ ID NO:11 or polynucleotides encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO:5 (or polynucleotide encoding SEQ ID NO:9), while allowing hybridization with the polynucleotide of claim 4 (or polynucleotide encoding SEQ ID NO:5 or SEQ ID NO:7).

Therefore, in light of the previously submitted claim amendments, and the remarks provided herein, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 3-5, 9, 10, 12-14, 16-25, and 38 under 35 U.S.C. §112, second paragraph.

35 U.S.C. §112, first paragraph- Written Description

The rejection of claims 3-5, 9, 10, 12-14, 16-25, and 38 under 35 U.S.C. §112, first paragraph for alleged lack of written description is respectfully traversed. Applicants respectfully disagree with the Patent Office's assertion that the "claim(s) contain subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (see page 4, paragraph 3 of the Office Action).

Specifically, Applicants respectfully submit that the claims and specification provide written description of the claimed invention, as evidenced, in part, by the explicit recitation of structural and functional properties for "peptide portions" of SMRT co-repressors. As amended in Applicants' communication submitted August 12, 2004, the present claims recite detailed structural (*i.e.*, SMRT co-repressor or peptide portion thereof having at least 80% sequence identity with SEQ ID NOs: 5, 7, or 9) and functional characteristics (*i.e.*, SMRT co-repressor or peptide portion thereof is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors) for polypeptides encoded by polynucleotides of the claimed invention.

Moreover, Applicants respectfully disagree with the Patent Office's assertion that "there does not appear to be literal support in the specification as originally filed for such a limitation" (see page 5, paragraph 1 of the Office Action). The Examiner's attention is directed to the specification at, for example, page 14, lines 23-27 which explicitly states:

> In another embodiment according to the present invention, there are provided polynucleotides encoding members of the above-described family of silencing mediators of retinoic acid and thyroid hormone receptor, or an isoform, **or peptide portion thereof (SMRT co-repressors)**, or an isolated polynucleotide complementary thereto (emphasis added in bold).

Thus, contrary to the Examiner's assertion, the specification provides literal support for polynucleotides encoding peptide portions of SMRT co-repressors.

Furthermore, Applicants respectfully disagree with the assertion by the Patent Office that "there is no basis provided in the specification or prior art for the skilled artisan to envision a representative number of specific embodiments to describe the broadly claimed genus of nucleic acids encoding literally any protein" (see page 5, paragraph 2 of the Office Action). Contrary to the assertion by the Patent Office that the claimed genus of nucleic acids encodes any protein, Applicants respectfully submit that the present claims are drawn to polynucleotides that encode a specified protein with an explicitly recited chemical structure (*i.e.*, an amino acid sequence having at least 80% sequence identity with SEQ ID NOs: 5, 7, or 9) and explicitly recited function (*i.e.*, capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors). Using guidance pertaining to structure and function provided in the claims and specification, it is within the scope of routine experimentation for one of skill in the art to make and use the claimed genus of polynucleotides.

Because the specification provides both structural and functional properties for the claimed genus of polynucleotides, Applicants respectfully submit that the specification describes all of the polynucleotides embraced by the claimed invention. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 3-5, 9, 10, 12-14, 16-25, and 38 under 35 U.S.C. §112, first paragraph.

35 U.S.C. §102(e)

The rejection of claims 4, 5, 9, 12, 19 and 21-22 under 35 U.S.C. §102(e) as allegedly being anticipated by Takashima et al. (U.S. Patent No. 6,248,559 B1), is respectfully traversed. To the extent that this rejection is premised on the Examiner's assertion that "[t]he claims are indefinite with regard to the phrase 'or a peptide portion thereof'" (see page 6, line 3 of the Office Action), the Examiner's attention is directed to page 8 *et seq* of the present communication where the definiteness of the claims is addressed in detail. In view of that discussion, the above-quoted assertion by the Examiner cannot support the present rejection.

Moreover, Applicants respectfully disagree with the Examiner's assertion that "the claims literally read on any nucleic acid encoding any protein sequence comprising any amino acid sequence that can be found in the reference sequence" (see page 6, lines 7-9 of the Office Action).

Contrary to the Examiner's assertion, Applicants' invention, as defined, for example, by amended claim 4, distinguishes over Takashima et al. by requiring an isolated polynucleotide encoding a SMRT co-repressor or a peptide portion thereof, or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor or peptide portion thereof is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein the SMRT co-repressor or peptide portion thereof comprises an amino acid sequence having at least 80% sequence identity with SEQ ID NO: 5.

Applicants' invention, as defined, for example, by amended claim 5, further distinguishes over Takashima et al., by requiring an isolated polynucleotide encoding a SMRT co-repressor or a peptide portion thereof, or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor or peptide portion thereof is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said SMRT co-repressor or peptide portion thereof is encoded by a polynucleotide having at least 80% sequence identity with SEQ ID NO: 4.

Applicants' invention, as defined, for example, by amended claim 9, still further distinguishes over Takashima et al., by requiring an isolated polynucleotide encoding a SMRT co-repressor or a peptide portion thereof, or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor or peptide portion thereof is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said SMRT co-repressor or peptide portion thereof is encoded by a polynucleotide having at least 80% sequence identity with SEQ ID NO: 7.

Thus, in order for a polynucleotide encoding a peptide portion of a SMRT co-repressor to be embraced by the present claims, the resulting peptide must meet both the structural and functional requirements set forth in the claims, i.e., it must be encoded by a polynucleotide having at least 80% sequence identity with SEQ ID NO: 4, 5 or 7 and be capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Takashima et al. do not disclose any such polynucleotides.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 4, 5, 9, 12, 19 and 21-22 under 35 U.S.C. §102(e).

CONCLUSION

In light of the remarks provided herein, Applicants believe that the present application is now in condition for allowance. Accordingly, prompt and favorable action on all claims is respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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